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09/362,598	07/28/1999	JOEL V. WEINSTOCK	3948/79934	7062
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EXAMINER				
ZEMAN, ROBERT A				
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03/21/2008		PAPER		

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

# Office Action Summary

## Application No.

09/362,598

## Applicant(s)

WEINSTOCK ET AL.

## Examiner

ROBERT A. ZEMAN

## Art Unit

1645

**Period for Reply** -- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 07 January 2008.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 24, 26, 28-32 and 36 is/are pending in the application.
- 4a) Of the above claim(s) 36 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 24, 26 and 28-32 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

## Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

## Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/C)
- 4) ☐ Interview Summary (PTO-413)
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_
- Paper No(s)/Mail Date \_\_\_\_\_

### **DETAILED ACTION**

Applicant's amendment and response filed on 1-7-2008 are acknowledged. Claim 24 has been amended. Claim 36 has been added. Claims 24, 26, 28-32 and 36 are pending. Newly submitted claim 36 is directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: the previously examined claims are drawn to methods of screening helminthic parasite preparations using fractionation and subfractionation without the addition of exogenous bioactive compounds. Newly added claim 36 utilizes the addition of exogenous bioactive compounds and consequently constitutes a patentably distinct method.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claim 36 is withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Claims 24, 26 and 28-32 are currently under examination.

### ***Claim Rejections Maintained***

#### ***35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The instant claims are drawn to a method of screening a helminthic preparation for one or more components that reduce a Th1 immune response. The method comprises preparing and fractionating and sub-fractionating the preparation and assaying the products for the ability to reduce a Th1 immune response.

The rejection of claims 24, 26 and 28-32 under 35 U.S.C. 103(a) as being unpatentable over Kullberg et al. (Journal of Immunology, 1992, Vol. 148, No. 10, pages 3264-3270 -- IDS) is maintained for reasons of record.

**Applicant argues:**

1. Kullberg et al. does not teach the step of seeking the active component of a helminthic parasite preparation by ANY method.
2. The Office action does not provide a description of the "negative effects" sought to be avoided.

3. Kullberg et al. does not teach the administration of a helminthic parasite as a therapeutic agent for decreasing a Th1 response.
4. A decreased Th1 response is not taught by Kullberg et al. as having a therapeutic effect. Thus the skilled artisan would not have been concerned with any alleged "negative effects".
5. The amended claims require that the helminthic parasite preparation is free of human bacterial, mycobacterial and viral pathogens.
6. New claims 36 has the additional limitation that myelin basic protein, PLP139-151, a super antigen, a mitogen, phorbol ester or a signal transduction analog be added prior to the step of assaying for a Th1 immune response.

Applicant's arguments have been fully considered and deemed non-persuasive.

With regard to Point 1, Applicant is reminded that the rejection was made under 35 U.S.C. 103(a) not 35 U.S.C. 102. The "seeking" of said active component is the basis of the obviousness rejection.

With regard to Point 2, the "negative effects" are any other than that which is being studied. Moreover, it is standard within the art to obtain as pure (homogeneous) preparation as possible when trying to determine the activity of a given composition.

With regard to Points 3-4, the therapeutic use of the claimed a helminthic parasite composition is not a limitation of the instant claims. Moreover, it is standard within the art to obtain as pure (homogeneous) a preparation as possible when trying to determine the activity of a given composition. When compositions comprising multiple components are used, one cannot determine which component is responsible for the observed effect. Therefore, contrary to

applicant's assertion, the skilled artisan would always be concerned with the effects that other components of a given composition might have.

With regard to Point 5, it would have been obvious for the skilled artisan to use a preparation that was free of exogenous antigenic material in methods measuring immune responses.

With regard to Point 6, claim 36 has been withdrawn from consideration and is under examination.

As outlined previously, Kullberg et al. disclose the helminthic parasite *Schistosoma mansoni* down regulates the Th1 cytokine secretion of IL-2 and IFN- $\gamma$  in mice (see abstract). Kullberg et al. further disclose that Th1 responses were determined by cytokine profiles as measured by *in vitro* ELISA assays (see materials and methods and results sections).

Kullberg et al. differs from the instant invention in that they don't disclose the method steps of fractionating, sub-fractionating and testing of the sub-fractionates. However, as attested to by Drs. Weinstock and Elliot in their Declaration filed under 37 C.F.R. 1.132 on 12-9-2005: "fractionation and testing of resulting fractions and sub-fractions for activity, as claimed, is a well-known and routine method for isolating the biologically active component(s) of a complex biological mixture. It is also well known in the art that the same assay can be used at each stage of a fractionation procedure to monitor which fraction(s) or sub-fraction(s) have the activity of interest" (see point 4 of Declaration). Consequently, in light of the KSR decision, it would have been obvious for one of ordinary skill in the art to use these "well known and routine methods" to identify the component(s) of the parasite composition responsible for the down regulation of Th1 cytokine secretion. One would have been motivated

to identify said component(s) in order to produce a “pure” composition capable of reducing a Th1 response without the possible negative effects of caused by the other constituents of the nematode composition. One would have had a reasonable expectation of success since said methods are well known and routine in the art (see *KSR International Co. v. Teleflex Inc.*, No. 04-1350 [U.S. Apr. 30, 2007]).

The rejection of claims 24, 26 and 28-32 under 35 U.S.C. 103(a) as being unpatentable over Lee et al. (WO 96/29802 – IDS) is maintained for reasons of record.

**Applicant argues:**

1. As pointed out previously, the data in table 1 of Lee et al. would lead the skilled artisan to determine that further purification of a helminthic parasite preparation would be unlikely to produce the result sought by the claims. This argument was merely “dismissed” by the Examiner with no rationale being provided.
2. The amended claims require that the helminthic parasite preparation is free of human bacterial, mycobacterial and viral pathogens.
3. New claims 36 has the additional limitation that myelin basic protein, PLP139-151, a super antigen, a mitogen, phorbol ester or a signal transduction analog be added prior to the step of assaying for a Th1 immune response.

Applicant’s arguments have been fully considered and deemed non-persuasive.

With regard to Point 1, contrary to Applicant’s assertion, the data in Table 1 would not lead the skilled artisan to determine that further purification of a helminthic parasite preparation

would be unlikely to produce the result sought by the claims as there is no statistical difference between the results using an extract or a live worm infection. Consequently, the skilled artisan would have been motivated to identify “active component” in order to obtain a “pure” composition in order to reduce the possible deleterious effects (i.e. non-specific immune responses etc). Since said compositions are administered to allograft (transplant) patients, the skilled artisan would necessarily want to minimize unwanted immune activators.

With regard to Point 2, it would have been obvious for the skilled artisan to use a preparation that was free of exogenous antigenic material in methods measuring immune responses.

With regard to Point 3, claim 36 has been withdrawn from consideration and is under examination.

As outlined previously, Lee et al. disclose the down regulation of Th1 activity in mice can be accomplished by the administration of soluble helminthic nematode extract (see page 5, line 21 to page 6, line 4 and page 10)). Lee et al. further disclose that Th1 responses were determined by cytokine profiles as measured by *in vitro* ELISA assays (see Example 2). Lee et al. differs from the instant invention in that it does not explicitly disclose the method steps of fractionating, sub-fractionating and testing of the sub-fractionates. However, as attested to by Drs. Weinstock and Elliot in their Declaration filed under 37 C.F.R. 1.132 on 12-9-2005: “fractionation and testing of resulting fractions and sub-fractions for activity, as claimed, is a well-known and routine method for isolating the biologically active component(s) of a complex biological mixture. It is also well known in the art that the same assay can be used at each stage of a fractionation procedure to monitor which fraction(s) or sub-fraction(s) have the activity of

interest” (see point 4 of Declaration). Consequently, in light of the KSR decision, it would have been obvious for one of ordinary skill in the art to use these “well known and routine methods” to identify the component(s) of the parasite composition responsible for the down regulation of Th1 cytokine secretion. One would have been motivated to identify said component(s) in order to produce a “pure” composition capable of reducing a Th1 response without the possible negative effects of caused by the other constituents of the nematode composition. One would have had a reasonable expectation of success since said methods are well known and routine in the art (see *KSR International Co. v. Teleflex Inc.*, No. 04-1350 [U.S. Apr. 30, 2007]).

### ***New Grounds of Rejection***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 24, 26 and 28-32 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Applicant has amended claim 24 to recite “a parasite preparation free of human bacterial, mycobacterial and viral pathogens...” This phrase does not appear in the specification, or original claims as filed. The portion of the specification set forth by Applicant as providing a specific basis for this limitation refers to the conditions under which the preparatory animals were raised not to the helminthic parasite preparations. Therefore this limitation is new matter.

***Conclusion***

No claim is allowed.

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ROBERT A. ZEMAN whose telephone number is (571)272-0866. The examiner can normally be reached on Monday- Thursday, 7am -5:30 p.m. .

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shanon Foley can be reached on (571) 272-0898. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>.

Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Robert A. Zeman/  
Primary Examiner, Art Unit 1645  
March 17, 2008